



Yellow fever vaccination for Chilean tourists visiting Brazil.

Practical considerations

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Vacuna contra fiebre amarilla para viajeros chilenos a Brasil. Consideraciones prácticas

La aparición de fiebre amarilla en las costas brasileñas, lugares de alto interés turístico, ha provocado una alta demanda de vacunación. Este artículo entrega respuestas a las principales consultas sobre la vacuna de fiebre amarilla y puede servir como guía para médicos no expertos en Medicina del Viajero.

Palabras clave: Fiebre amarilla, vacuna, Medicina del Viajero, Brasil, brote.

Keywords: Yellow fever, vaccine, Travel Medicine, Brazil, outbreak.

Brazil is among the main touristic destinations for Chileans with more than 280,000 travelers registered in 2017. The recent introduction of yellow fever (YF) into the coastal regions from Bahia southwards, including Brazil's main touristic cities, is a mayor challenge for physicians working in Travel Medicine and vaccination centers in Chile and elsewhere. The threat of YF for travelers is not only theoretical as demonstrated by the recent cases in unvaccinated travelers from different countries including two fatal cases in Chilean travelers visiting Isla Grande¹. In general, visitors to endemic regions are advised to receive the vaccine beforehand; this is even more important for visits to the newly affected coastal regions in Brazil with the higher and unpredictable risks of an outbreak situation.

The question of which traveler needs YF vaccination is a classical topic of Travel Medicine, requiring detailed information on the global distribution of YF and the entry requirements of each of the visited countries. YF vaccine aims to prevent travelers from suffering severe YF manifestations, which have a very high fatality rate. Of the 10 cases of travel-related YF, reported between 1979 and 2002 in the literature, only two survived². The administration of YF vaccine is complicated by two aspects; 1) due to the necessity of a strict cool chain and the legal issues regarding the vaccination certificate, only a limited number of vaccination centers are licensed to administer the vaccine, and 2) YF vaccine is a live attenuated vaccine with a risk of severe side effects, therefore requiring an individual risk-benefit evaluation of each traveler to endemic regions or countries that require YF vaccination at entry³. As an additional problem, the production capacities of YF vaccine are limited by the complexity of the fabrication.

Due to the increasing number of epidemics, the spread

to new geographical areas, and the raise in exposed and infected people over the last two decades, the availability of YF vaccine is an emerging problem in various countries including Chile, which most probably will persist in the near future.

The ongoing YF outbreak in Brazil causes a massive increase of people requiring YF vaccination in Chile. Many of these are tourists visiting coastal Brazil often with their families and mostly for rather short periods of time. Sao Paulo and Rio de Janeiro are also frequent itineraries for business trips from Chile. As a consequence, many physicians who are inexperienced with Travel Medicine will be confronted with questions of patients planning to visit Brazil.

The following advices summarize some of the relevant practical issues for non-expert physicians in Chile and elsewhere.

• How should travelers to Brazil plan to get vaccinated?

Since the supply with YF vaccine in Chile is unstable and not predictable, travelers planning to travel to Brazil (or other itineraries requiring YF vaccination) should seek travel advice way ahead (ideally various months).

• Is YF vaccine obligatory to travel to Brazil?

Brazil does not require yellow fever vaccination (or any other vaccine) to enter the country. Still, to be protected from infection, all travelers to the affected areas should be vaccinated. In addition, travelers should also follow recommendations for the prevention of mosquito bites.

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Conflictos de interés: ninguno.
Financiamiento: ninguno.

Recibido: 16 de octubre de 2018.

Aceptado: 21 de octubre de 2018.

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- **How to respond if travelers ask if YF vaccine is really necessary?**

Travelers should be informed about the severity of yellow fever, which might manifest as a hemorrhagic fever with case-fatality rates comparable with Ebola virus infection. Infected mosquitos transmit the infection. Mosquito bites are unavoidable in tropical regions even if repellents and other measures are used. The epidemiological risk of infection depends on various factors and is unpredictable especially if the disease is introduced into a new region (as in coastal Brazil). As a logical consequence, any person entering to a risk area should be vaccinated beforehand.

- **How effective is the vaccine? Can travelers get infected despite being vaccinated?**

The exact effectiveness of YF vaccine is not known since controlled clinical trials have not been performed. Still, based on the epidemiological data and clinical experience, the vaccine is considered one of the most effective vaccines available. In the last 70 years more than 500 million people have been vaccinated and only 18 cases of vaccine failure have been reported⁴.

- **Should travelers visiting areas in Brazil without YF risk or pass through the airports in Sao Paulo or Rio de Janeiro receive YF vaccine?**

For travelers planning to travel exclusively to regions in Brazil without risk of YF, the vaccine is not indicated. The same applies for airport stopovers in Sao Paulo or Rio de Janeiro.

- **What have physicians to be aware of if they prescribe YF vaccine?**

Physicians providing prescriptions for YF vaccine have to evaluate each patient for possible contraindications and precautions, and advice the traveler on possible side effects and avoidance of pregnancy (> 1 month after vaccination). Travelers with contraindications cannot receive the vaccine; those with possible contraindications or precautions (Table 1) should be evaluated on an individual basis by a physician with expertise in Travel Medicine.

- **When is the best time to get vaccinated?**

Antibody production starts approximately 5 days after vaccine administration and reaches protective levels after 10 days. Therefore, travelers receiving the vaccine 10 days before going to risk areas in Brazil are considered protected. Still, if there is sufficient time, it is advisable to receive YF vaccine 4 weeks or more before travelling.

- **What to do if a traveler is not sure if he has received YF vaccine before in his life?**

If the YF vaccination status is uncertain, the traveler should receive the vaccine. Repeated vaccinations within any timespan are not associated with a higher risk of adverse effects, in contrary, revaccinations have a lower risk of side effects.

- **How long does the vaccine protect? Which travelers need a revaccination or booster?**

According to recent WHO recommendations, YF vaccine provides long-term, life-long protection and the vaccination certificate is valid for life³. This new guideline also includes YV vaccination in the past (since the vaccine has not changed in the last 70 years). According to international Travel Medicine experts, the WHO recommendation applies to most travelers, but certain groups might benefit from revaccination after 10 years^{4,5}. Which traveler might need such a booster is still controversial (Table 2 lists possible factors favoring revaccination). If some tourists traveling to Brazil, who received YF vaccine > 10 years before, should be revaccinated, might be evaluated on an individual basis by a Travel Medicine expert.

- **What to do if travelers present less than 10 days before traveling?**

YF vaccine should be given at least 10 days before entering YF risk zones (see above). If travelers present

Table 1. Contraindications and precautions for yellow fever vaccine

Contraindications	- Age < 6 months - Breastfeeding women of infants < 6 months of age or of severely immunocompromised infant - Severe immunodeficiency* - Severe egg allergy
Precautions**	- Age 6-9 months - Breastfeeding of infants 6-9 months of age - Age > 60 years - Pregnancy - Minor immunodeficiency

*Primary immunodeficiencies, thymus disorder, symptomatic HIV infection or CD4 T-cell values < 200 per μ L, recent chemotherapy (for malignancies) or radiation targeting immune cells or hematopoietic stem cell or solid organ transplantation, treatment with immunosuppressive or immunomodulatory drugs (e. g. high dose corticosteroids, alkylating drugs, antimetabolites, TNF-inhibitors, IL-1 blocking agent, or other monoclonal antibodies targeting immune cells)³.

**Vaccination only after individual risk-benefit evaluation by experienced physician.



with less than 10 days of anticipation and travel cannot be postponed, they should receive the vaccine, but be advised that protection is incomplete and strict mosquito bite avoidance is crucial.

• **Is it useful to screen for YF antibodies to see if a patient has been exposed in previous travels?**

No, this approach is not recommended. Even if a traveler might have been exposed to YF virus before, he should also get the vaccine if traveling to risk areas.

• **How to administer YF vaccine together with MMR or vaccines?**

The Chilean Ministry of Health recommends that the following Chileans receive measles-mumps-rubella (MMR) vaccine before international travel: those born between 1971 and 1981, children with only 1 dose of MMR (age 13 month to 7 years), and unvaccinated children aged 6 to 12 months. Travelers requiring both, YF and MMR vaccine, should receive the vaccines with >30 days of separation or on the same day. If both options exist, separated vaccination is preferable, because of possible interference⁶. Inactivated vaccines such as hepatitis A and B, typhoid fever, influenza, tetanus/diphtheria/pertussis or rabies vaccines can be administered on the same day or at any time interval with YF vaccine.

• **What to do if a traveler to Brazil has recently received MMR vaccination?**

There is no standard answer to this question. The coadministration of YF and MMR vaccine without 30 days of separation is safe, but might affect the immune response to the vaccines⁶. Travelers, who need to be vaccinated against YF but received MMR vaccine within the last 30 days, should be evaluated and counseled by a Travel Medicine expert. The same applies if a patient has received YF vaccine and also has an indication for a MMR booster without time to separate the vaccines by 30 days.

• **How to know if YF is present in a certain area in Brazil?**

The epidemiological situation of yellow fever in Brazil (and other countries) has been very dynamic in recent years. Physicians providing advice regarding YF vaccination should check regularly for up-to-date

Table 2. Factors favoring yellow fever booster vaccination (after 10 years or earlier)

Factor	Reference
Pregnancy (at time of first vaccination)	4, 8
HIV-infection (at time of first vaccination)	4, 8, 9, 10
Any immunodeficiency (at time of first vaccination)	8
Hematopoietic stem cell transplant recipient	4, 8
Stay in region with active YF outbreak	4
High YF risk due to activities, travel season or long-term stay in endemic area	4, 9
Laboratory workers who handle wild-type YF virus	4
Vaccination with Brazilian vaccination strain (17DD-YF)	11
Vaccination at age < 2 years	8, 9, 10
YF vaccine applied together with MMR	6

Table 3. Links with epidemiological information regarding yellow fever

Centers of Disease Control and Prevention. Yellow Fever Maps. Available at: https://www.cdc.gov/yellowfever/maps/index.html
PAHO/WHO. Yellow Fever: Epidemiological Alerts and Updates. Available at: https://www.paho.org/hq/index.php?option=com_topics&view=rdmore&cid=2194&Itemid=40784&lang=en
European Centre for Disease Prevention and Control. Yellow fever. Available at: https://ecdc.europa.eu/en/yellow-fever

epidemiological information using reliable internet sources (Table 3). Informal sources, e.g. internet groups or non-expert colleges, should not be consulted. It can be anticipated that the newly affected coastal regions in Brazil (including main touristic areas) will stay YF risk areas for the next years or decades.

• **What is the fractional dose of YF vaccine?**

Fractional dosing is an emergency measure that helps to vaccinate more people in situations of limited YF vaccine stock. According to experts, the use of a split dose (one fifth) protects for at least 12 months and can be used for individuals >2 years of age in emergencies such as outbreaks. Some countries (e.g. Canada) have also used this approach in times of limited vaccine access to vaccinate travelers⁷. The decision to offer fractional dose YF vaccine in certain situations depends on the health authorities and the respective vaccine centers and not on individual physicians. The precautions and contraindications are the same as for the full dose. A fractioned dose does not entitle to receive the international yellow fever certificate.



• What to do if YF vaccine is not available?

There is no standard answer to this question. If the vaccine is not available and the journey cannot be postponed or changed, the traveler should seek advice on the individual risk and on the options of risk reduction by a Travel Medicine expert.

• Do travelers to Brazil who cannot receive YF vaccination benefit from a “waiver letter”?

No, waiver letters are useful for travelers with contraindications or precautions, who visit countries, usually without YF risk, which require YF vaccination certificates at entry. Brazil does not require such a certificate, but as mentioned above, travelers should avoid visits to risk areas in Brazil if unvaccinated.

Conclusions

Physician without expertise in Travel Medicine might prescribe YF vaccine to tourists to Brazil if they visit areas of YF risk, but should carefully evaluate each of them for recent vaccines, age, pregnancy, medications, and morbidities. In the following situations, the traveler should be referred to an expert in Travel Medicine:

- If the patient has possible contraindications or precautions (see Table 1).
- If the patient has received YF vaccine >10 years ago and there are questions about the usefulness of revaccination (see Table 2).
- If YF and MMR vaccine are both indicated but cannot be given on the same day nor separated by more than 30 days.

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